Seminars in Dialysis

TRANSITION TO DIALYSIS:
CONTROVERSIES IN ITS TIMING AND MODALITY

Dialysis Initiation: What's the Rush?

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ABSTRACT

The recent trend to early initiation of dialysis (at eGFR >10 ml/min/1.73 m^2) appears to have been based on conventional wisdoms that are not supported by evidence. Observational studies using administrative databases report worse comorbidity-adjusted dialysis survival with early dialysis initiation. Although some have concluded that the IDEAL randomized controlled trial of dialysis start provided evidence that patients become symptomatic with late dialysis start, there is no definitive support for this view. The potential harms of early start of dialysis, including the loss of residual renal function (RRF), have been well documented. The rate of RRF loss (renal function trajectory) is an important consideration for the timing of the dialysis initiation decision. Patients with low glomerular filtration rate (GFR) may have sufficient RRF to be maintained off dialysis for years. Delay of dialysis start until a working arterio-venous access is in place seems prudent in light of the lack of harm and possible benefit of late dialysis initiation. Prescribing frequent hemodialysis is not recommended when dialysis is initiated early. The benefits of early initiation of chronic dialysis after episodes of congestive heart failure or acute kidney injury require further study. There are no data to show that early start benefits diabetics or other patient groups. Preemptive start of dialysis in noncompliant patients may be necessary to avoid complications. The decision to initiate dialysis requires informed patient consent and a joint decision by the patient and dialysis provider. Possible talking points for obtaining informed consent are provided.

Recently, Rosansky et al. reviewed the trend to early initiation of dialysis, defined as estimated glomerular filtration rate (eGFR) of >10 ml/min/1.73 m^2 (1,2). They were unable to find a mortality, morbidity, or quality of life benefit of early dialysis initiation. Molnar et al. found no benefit of early versus late dialysis initiation in incident dialysis patients as well as patients returning to dialysis after failed transplant (3). Herein, we further examine the potential harms of early dialysis initiation versus benefits. We believe that this analysis supports the view that in most cases, starting dialysis as late as possible, excluding potentially life-threatening renal failure complications or other exceptions (as will be discussed) are the best evidence-based strategy.

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TABLE 1. Controversial conventional wisdoms that may be used to justify early dialysis start

1	Level of dialytic clearance of low-molecular-weight solutes (e.g., urea) is associated with a survival/morbidity benefit and is comparable to endogenous renal function
2	Low albumin and nutritional issues are synonymous
3	Nutrition can be improved with increased dialytic clearance of low-molecular-weight solutes (e.g., urea)
4	Diabetics need to initiate dialysis earlier than nondiabetics
5	At low levels of renal function, i.e., eGFR <15 ml/min per 1.73 m^2, most nephropathies progress relentlessly to minimal kidney function
6	Waiting until eGFR is <6 ml/min per 1.73 m^2 to initiate dialysis is potentially dangerous
7	IDEAL study demonstrates that the majority of patients will become symptomatic (uremic) if dialysis is postponed to eGFR levels of 5–7 ml/min/1.73 m^2
8	MDRD eGFR is inaccurate and thus not useful in the dialysis initiation decision
9	Frequent hemodialysis or incremental dialysis initiation may overcome some of the harm associated with early dialysis initiation and thus should be offered to new dialysis early starts

eGFR, estimated glomerular filtration rate derived from the 4-variable Modification of Diet in Renal Disease (MDRD) formula.

The trend to early start of dialysis can be related to six conventional wisdoms (Table 1) (1). Three new justifications have surfaced which will be examined. These include the conclusion that the IDEAL study provided evidence that all patients will have dialysis justifying "uremic" symptoms at eGFR less than 10 ml/min/1.73 m^2 (4). Second, that eGFR is an inaccurate, and thus not useful, parameter in the dialysis initiation decision (5,6). Lastly, that utilization of more frequent or incremental dialytic schedules should be considered as a way to decrease the adverse consequences of early dialysis initiation (7).

Several considerations in the early start debate have not been fully explored, including the relationship of acute kidney injury (AKI) or congestive heart failure (CHF) with early initiation and the use of early start for noncompliant patients or as an elective procedure to accommodate dialysis-related technical issues.

Recently, the American Society of Nephrology has promoted the concept of joint decision making for dialysis initiation by patients, their families, and dialysis providers (8). In an effort to promote this concept, theoretical talking points for this discussion will be presented that incorporate the information presented.

Controversial Conventional Wisdoms Driving Early Start of Dialysis

Increased Dialytic Clearance of Toxic Uremic Solutes by Dialysis Provides a Survival/Morbidity/Quality of Life Benefit

The first study to examine the association of dialytic small molecule (urea) clearance to survival was the National Cooperative Dialysis Study published in 1981 (9,10). This study of 151 patients followed up for 6 months found no significant difference in survival with higher urea clearance, and a borderline significant difference in hospitalizations.

Hakim and Lazarus advanced the concept that dialytic clearance is equivalent to endogenous renal clearance and should be considered in the dialysis initiation decisions in 1995 (11). In 2002, two randomized controlled studies, one in hemodialysis and the other in peritoneal dialysis, both in patients with minimal RRF, failed to show a benefit of greater dialytic small molecule clearance on survival (12,13). One could argue that if the additional contribution of small molecule clearance to the minimal level of RRF in the patients from these randomized controlled trials did not provide a survival benefit, then adding similar or smaller amounts of dialytic clearance to early starts would be even less likely to provide a survival benefit.

Nutritional Decline can be Treated with Early Dialysis Initiation and Low Serum Albumin is an Indicator of Nutritional Problems

The view that nutritional decline is a reason to initiate dialysis may have been the most important driver of the trend to early start (11,14). The majority of national and international guidelines since 1997 have promoted this nutritional indication for early dialysis (14). One could argue that this suggestion explains why nutritional deterioration was given as the most important reason for early initiation of dialysis in a 1999 survey of European nephrologists (15). A full analysis of the nutritional issue is beyond the scope of this review. Studies that examine this issue in incident dialysis populations give conflicting results (16–18). Although dialysis initiation is generally associated with higher intake of calories and dietary protein, the reasons for this effect remain unclear (18). It may be that dietary restriction is lifted after dialysis initiation. Although serum albumin may increase in the short-term after dialysis initiation, neither lean body mass nor other markers of body protein stores have been shown to increase.

Several studies have affirmed that serum albumin is not a reliable nutritional marker and that serum albumin levels do not relate to objective indices of nutrition (19).

Despite the lack of data supporting a benefit of starting dialysis for a decreasing serum albumin or any benefit of early start on nutrition, a 2012 publication found that 53% of nephrologists would start dialysis immediately, with a dialysis catheter, if a patient showed evidence of deteriorating nutritional status (20).

Patients with Diabetes Benefit from Early Dialysis Initiation

It is difficult to trace the source of the widely held belief that patients with diabetes benefit from early dialysis initiation. This view continues to be included in the majority of national and international dialysis initiation guidelines (14). Studies using national and international registries show that the association of early start with higher mortality is stronger among patients with diabetes than in nondiabetic dialysis patients (21).

Once Patients' RRF Reaches 30 ml/min/1.73 m^2, Patients Will Progress Relentlessly to Very Low Levels of GFR

In a review of papers that examined renal function change over time (Renal Function Trajectory; RFT), Rosansky presented evidence that a large segment of the Chronic Kidney Disease (CKD) 3–5 population may have a slow decline or no decline over many years (22). This view was reinforced by reports on patterns of change in kidney function from the AASK trial involving African American patients with "hypertensive nephrosclerosis" (23,24). In 40% of these patients, followed up for an average of 9 years, kidney function was either stable or showed a nonlinear change over time. Elderly patients may be more likely to have a stable RFT pattern (25,26). Thus, the decision to initiate dialysis early in the elderly CKD stage 5 population, with limited life expectancy and slow or no decline in renal function, is not supported by available evidence (26).

The most recently published guidelines for dialysis initiation from Europe recommend consideration of the RFT in the decision to initiate dialysis (27), although these guidelines also convey the expectation of relentless decline of renal function. In addition, they promote preemptive start of dialysis in diabetics and in patients who cannot be followed up closely enough to detect a decline of renal function to a dangerously low eGFR, of approximately 6 ml/min/1.73 m^2 (27).

Patients with Advanced CKD (Stage 5) Become Symptomatic When eGFR is Less Than 6 ml/min/1.73 m^2 Constituting an Absolute Indication for Starting Dialysis

Guidelines that recommend dialysis before GFR of 6 ml/min/1.73 m^2, include 2002 European, 2009 United Kingdom, and 2005 Australia/New Zealand guidelines (14). This recommendation assumes linear or relentless loss of renal function and also that patients are likely to have life-threatening symptoms at this level of renal function. As mentioned above, a significant segment of the CKD stage 4 and 5 populations may be asymptomatic and have stable but low levels of renal function for years.

Data on patient symptoms in relation to the levels of renal function are scarce. Murtagh et al. did not find any reports of symptoms among patients with CKD stage 4/5 not on dialysis (28). Di Micco et al. published one of the only studies that examined this issue in a small population of patients, who had a low burden of comorbidity, and were on a low-protein diet (29). Thus, the findings from this study may not apply to CKD stage 5 patients with higher comorbidity and on higher protein intakes. Nevertheless, these researchers produced a list of specifically defined renal failure-related clinical signs, symptoms and chemistry values that justified dialysis start. Patients were enrolled when eGFR was <11 ml/min/1.73 m^2 and dialysis was started if one of these findings occurred or if eGFR reached 6 ml/min/1.73 m^2. Only 7 (23%) of the 30 patients in the study had any of the nine clinical reasons to initiate treatment after 23 months of follow-up; 14 (47%) of these patients reached an eGFR of 6 ml/min/1.73 m^2 without dialysis- requiring symptoms and 8 (27%) did not initiate dialysis after 23 months of follow-up (29).

One study examined the relationship between uremic symptoms at dialysis initiation and outcomes (30). The most common symptom was loss of appetite at an eGFR of 4.75 ml/min/1.73 m^2. Other reasons to start dialysis included intractable edema, oliguria or neuropathy; each occurred in only 5–6% of the patients who initiated dialysis at an eGFR of 4.5–6.1 ml/min/1.73 m^2. No associations between symptoms and survival were observed in this study.

The IDEAL study influenced the development of the most recent European guidelines on the timing of dialysis initiation (27,31). A large proportion of patients assigned in the IDEAL trial to late start of dialysis (defined as an eGFR of 5–7 ml/min/1.73 m^2) were started earlier (with an eGFR above 10 ml/min/1.73 m^2) with the most frequent reason "uremia" (4). Unfortunately, the lack of detail makes it difficult to evaluate the specificity (true uremia) and severity of symptoms. A more likely explanation for the crossovers to early start may have been guidelines emanating from Australia/New Zealand stating that dialysis needed to be started before an eGFR of 6 ml/min/1.73 m^2 (14).

From the above studies on symptoms versus GFR level, true uremia seems an unlikely cause of the majority of these crossovers to early start. Late start in IDEAL was not associated with any adverse outcomes. Thus, we do not interpret the results of IDEAL as warranting a recommendation to start dialysis at a GFR above 5–7 ml/min/1.73 m^2 in the absence of symptoms.

Should eGFR be Considered in the Dialysis Initiation Decision?

In a recent study, 54% of nephrologists considered the level of measured (or estimated) renal

function to be the most important criterion for dialysis initiation in uncomplicated patients (20).

Two papers, questioned the validity of the inverse relationship between starting levels of eGFR (equations based on serum creatinine concentration) and comorbidity-adjusted survival (5,6). Grootendorst et al., using data from the NECOSAD study, found that renal function as measured by the average of timed endogenous urea and creatinine clearances, did not show the relationship between this measured eGFR and survival (5). In this study, patients were primarily started late (eGFR less than 5 ml/min/1.73 m^2). Although the adverse outcome of early start with higher eGFR was not seen when using the 24-hour urine approximation of GFR, neither was there a benefit of starting at an eGFR of approximately 8 ml/min/1.73 m^2 versus an eGFR of 3 ml/min/1.73 m^2.

A similar result was shown by Beddhu et al. in a sample of the US dialysis starts between 1996 and 1999 (6). The survival disadvantage of early start as determined by eGFR (creatinine-based) was no longer present when data from 24-hour urine endogenous creatinine clearance were used. As in the report by Grootendorst et al. there was no benefit of starting dialysis early when creatinine clearance data were used.

Although mean urea and creatinine clearance based on 24-hour urine collection has been advocated as a way to obtain more accurate GFR estimates, Frontseré et al. found that MDRD eGFR (creatinine-based) was a more accurate measure of true GFR (51Cr-EDTA clearance) than the 24-hour creatinine–urea clearance urine estimate (32).

Some early start patients have falsely high eGFR (creatinine-based) as a result of low muscle mass and resultant low creatinine production for their age (1). Low muscle mass (sarcopenia) correlates with morbidity and other quality of life (such as frailty) indicators. Nevertheless, longitudinal eGFR (creatinine-based) data have value as long they are interpreted in light of a patient's unique clinical context. For example, nephrologists can look at longitudinal weight, subjective global assessment, and mid arm circumference data to help decide if a current eGFR value is excessively confounded by muscle loss. If patients do not have evidence of muscle mass loss, longitudinal eGFR data can be of value in determining RFT and RRF. However, a single eGFR value should not be used to decide when to initiate dialysis. Rate of loss of renal function, validated by measurements over several years, could aid in determining who needs dialysis, when to begin preparation for dialysis therapy, and how quickly dialysis needs to be initiated (22).

Patients who demonstrate unequivocal loss of muscle mass and thereby stable (but falsely so) values for eGFR (creatinine-based) are likely to have a poorer prognosis than patients with retention of a constant muscle mass as true GFR declines. In the study by Beddhu, patients who had a falsely high eGFR often needed assistance with ambulation and eating, both potential predictors of mortality (6). For these debilitated and frail patients with other associated comorbidities, especially the elderly, and for patients of any age with a short life expectancy, conservative management may provide a better quality of life, and in some cases, longer hospital free survival compared with dialytic management (33).

Should Frequent Hemodialysis or Incremental Hemodialysis Be Considered as a Way to Improve Outcome with Early Dialysis Initiation

Recently, Rosansky and McIntyre questioned the idea of considering frequent hemodialysis as a means to counter the problems related to early dialysis initiation (7,34). As preservation of a patient's RRF is crucial, use of more frequent dialysis should only be considered in patients with minimal RRF (late dialysis initiators). This subset may benefit by a reduced left ventricular mass with frequent daily treatments (35), but a survival benefit has yet to be convincingly shown. In contrast to these patients, Rocco et al. reported no benefit of frequent nocturnal hemodialysis, possibly because this study included incident dialysis patients who have significant RRF (36). Frequent hemodialysis in patients with minimal RRF may be beneficial by improving quality of life for some patients (37).

Similarly, incremental hemodialysis has been advocated as a way to decrease the potential harm associated with dialysis initiation. If patients have significant RRF, the amount of small molecule clearance with short infrequent dialysis treatments is unlikely to add to their total clearance.

Dialysis large molecule clearances are much lower than 24-hour endogenous large molecule clearance. Dialysis membranes remove low molecular weight (MW) toxins (MW <500 kDa) far better than larger species, but the native kidney filters all equally up to a MW 68,000 kDa (38), which includes fragments of large biologically active molecules such as cell surface receptors and cytokines (39). A biologic kidney with a GFR of 10 ml/min will provide a continuous clearance of about 10 ml/min for small and larger MW toxins. A dialytic small molecule clearance of 10 ml/min, however, will be accompanied by larger MW clearances of as little as 1–2 ml/min.

"First Do No Harm", The Dangers and Risk of Early Dialysis Versus Mortality Morbidity or Quality of Life Benefit

In a meta-analysis of papers published between 2001 and 2011, Susantitaphong et al. found that a 1 ml/min/1.73 m^2 higher starting eGFR was associated with a 3–4% higher adjusted hazard ratio for all cause mortality (40). Higher comorbidity is associated with earlier initiation of dialysis in the international studies that have examined this issue. Elderly subjects often start at higher eGFRs and

often have very high comorbidity. Although unproven, one way to delay start of dialysis in these elderly high comorbidity patients is to use a low-protein diet. This approach might delay the need to start dialysis until eGFR reaches <5 ml/min/1.73 m^2 (29,41).

With regard to morbidity, McIntyre and Rosansky reviewed the multitude of risks that a patient who is given true informed consent (Table 2) needs to understand before he/she chooses to initiate dialysis (34).

Loss of a patient's endogenous renal function is an important issue to consider. Dialytic clearance has not been demonstrated to have mortality, morbidity, or quality of life benefit, whereas a patient's RRF, even at levels below 5 ml/min/1.73 m^2, is clearly beneficial (42,43), perhaps be aiding in regulation of extracellular volume. The loss of RRF with both peritoneal and hemodialysis (possibly less with the former) has been well documented (44). Patients may lose approximately 10% of their endogenous renal function per month after dialysis initiation (44). Recently the concept that loss of renal function after dialysis initiation is faster than the rate of loss prior to initiation has been challenged (45).

Adverse cardiovascular events associated with dialytic therapy have been well demonstrated (46,47). Recently, Assa et al. demonstrated that shortly after hemodialysis treatment begins, regional left ventricular systolic dysfunction may occur (48).

Sudden death accounts for about a quarter of dialysis patient mortality (49,50). It has been suggested that shorter treatment times and larger ultrafiltration volumes relate to sudden death. This hypothesis was supported by the data of Jadoul et al. in an analysis of Dialysis Outcomes and Practices Study data (51). The hazard ratio for sudden death was 1.13 for short treatment timer, 1.15 for large ultrafiltration volume and 1.10 for lower Kt/V. Low K+ concentrations in the dialysate were also associated with sudden death (51).

Infections are another serious adverse consequence of dialysis initiation. Examining data from approximately 300,000 patients treated between 1997 and 2009, Chan et al. found a very high death rate at 2 weeks, which persisted until 90 days after dialysis initiation (52). Patients with dialysis catheters were more likely to be in these early death groups. Although not specifically reported by Chan, dialysis catheter infection may account for a large proportion of these deaths. This hypothesis is supported by Lacson et al. who found using data from approximately 78,000 prevalent dialysis patients, that central venous catheter dialysis versus arteriovenous (AV) access dialysis, increased the likelihood of hospitalization and death by 45% and 39%, respectively (53).

Regarding quality of life, there have been no data to show that early start of dialysis improves quality of life, especially in the frail elderly (54). Conversely, many studies have shown adverse quality of life effects of dialysis initiation (55,56). Patients on dialysis have a high symptom burden including lack of energy, tiredness, dry mouth or thirst, pruritus, numbness, sleep disturbance, cramps, dyspnea, headaches, joint pains, depression and anxiety (28). Improved self-reported physical health and

TABLE 2. Information that can be provided to patients during shared decision making for dialysis initiation

1	You have been losing weight and muscle mass. Your appetite may improve once we start dialysis, but dialysis itself may worsen your loss of muscle and has not been shown to have a long-term benefit for your nutritional problems
2	Many studies have been published that have either demonstrated no survival benefit of early dialysis initiation or worse survival by starting now versus waiting until your remaining kidney function is much lower
3	One potential reason to delay your dialysis start is that you have x percent of your own renal function left. Once you start dialysis, it is very likely that this residual kidney function will be lost
4	Your residual kidney function has been shown to provide survival benefits and is superior to the artificial kidney function from your dialysis treatment
5	Starting your dialysis treatments with a dialysis catheter and not a working AV access may lead to a life-threatening infection. Delaying your dialysis until you have a working AV access may result in symptoms of renal failure. Nevertheless, it has not been shown that these symptoms will be life threatening. We can monitor these symptoms in our predialysis outpatient clinic and delay your dialysis treatment until you have a working dialysis access and these symptoms are no longer manageable without dialysis
6	You have adequate renal function and do not have symptoms directly related to low levels of kidney function. Nevertheless, you have a bad heart (liver) and we can start dialysis to help keep fluids out of your lungs. Using dialysis rather than maximum fluid removal medicine has not been shown to be a superior way to manage this problem
7	You have not been adherent to your medical regimen resulting in dangerously high levels of blood pressure, potassium, and excess fluid in your lungs. Because of these dangerous situations, I would like you to consider starting your dialysis now
8	Your kidney function has temporarily worsened. Medical treatments may get your kidney function to your baseline or you can consider dialysis start now
9	You have a rapid loss of kidney function that will not slow regardless of all of the treatments we have tried. Starting dialysis may avoid an emergency situation where we will have to start dialysis under conditions that might endanger your life
10	Start of dialysis early may help your dialysis access/home peritoneal dialysis work better, but there is no proof that this will improve your survival
11	When you start dialysis, you may want to consider 5–7 treatments per week instead of the usual 3 treatments per week. This frequent dialysis may result in you needing more surgeries for dialysis access, but it may improve the quality of your life
12	You are aware that you have low kidney function. Nevertheless, because of your age and your multiple other life-threatening conditions, you may be more likely to die of a nonkidney failure-related issue before your kidney function gets low enough to cause your death

functioning may occur in some patients treated with frequent in-center hemodialysis (37). No quality of life benefits were reported with nocturnal frequent dialysis (36). The trend to higher discontinuation rates in patients who initiate dialysis at higher starting eGFRs, especially the elderly, may be related to the decreased quality of life and high symptom burden that these patients experience (55–57).

Early Start and Nonuremia Issues

AKI and the Dialysis Initiation Decision

Studies that include national and international dialysis registry data do not track longitudinal eGFR. The frequency of early dialysis initiation after an episode of acute AKI needs further study. One small study found approximately 10% of new starts occurred after an AKI episode (58). O'Hare et al. found that approximately one-third of these patients had an eGFR >30 ml/min/1.73 m^2, 2 years prior to dialysis initiation (59). Patients who had a predialysis initiation AKI, as assessed by Medicare discharge diagnosis data, had higher predialysis initiation eGFR and had a worse postdialysis initiation survival. Unfortunately, longitudinal eGFR data were not available. Thus, this study could not examine how AKI impacts the relationship between higher dialysis initiation eGFR and mortality. In one study of sepsis-related AKI, early start of dialysis did not appear to be beneficial (60).

Congestive Heat Failure and Early Dialysis

Patients with CHF may start dialysis early due to fluid management issues. In a recent report, fluid overload in heart failure patients, treated with isolated dialytic ultrafiltration, was not superior to aggressive diuretic therapy (61). The relationship between the cardio-renal syndrome and early dialytic therapy needs to be explored (62). Patients with low urine output despite aggressive diuretic therapy may need to begin dialysis early.

Does Planned Dialysis Start Justify Early Dialysis Initiation?

Many patients are noncompliant with their predialysis regimen. In some of these patients, early start of dialysis may be planned after recurrent episodes of fluid overload, uncontrolled hypertension, or other symptoms (63). de Jager et al. and Mendelssohn et al. reported on the adverse consequences of late referral to a nephrologist and unplanned dialysis starts, respectively (64,65). In some cases, peritoneal dialysis patients are started on dialysis early in an incremental fashion with the addition of more dialysis time as residual GFR declines. In a recent report of results from the IDEAL study, patients assigned to late start were less likely to utilize planned peritoneal dialysis therapy (66). Early start of peritoneal dialysis was not superior to late start in one recent report (67). Whether the potential benefits of early incremental peritoneal dialysis outweigh the adverse impact of early start remains unclear.

Late as Possible Dialysis Start Should be the Default Position

Rosansky et al. showed in an observational study that, for patients with low comorbidity, starting dialysis as late as possible appeared to be beneficial (68). The study included "healthy" patients (zero reported comorbidity, except hypertension, no diabetes and under age 65 years) and thus may not be applicable to other populations. This study may have been confounded by unmeasured (i.e., frailty (69,70)) or incorrectly measured comorbidities, as well as survivor bias (healthier patients survive to lower levels of eGFR compared with sicker patients). Nevertheless, an examination of data on dialysis initiation versus starting level of renal function support the view that for patients without a predialysis episode of AKI or CHF, dialysis start should be delayed as long as a patient remains free of definitive uremia-related symptoms. Hwang et al. have shown that for their patients dialyzed in Taiwan, late start (as low as an eGFR of 3 ml/min/1.73 m^2) showed better comorbidity-adjusted survival than patients who started at an eGFR of approximately 6 ml/min/1.73 m^2 (70). Thus, it remains to be determined what the lower level of GFR is at which dialysis is absolutely indicated.

The shared decision for dialysis initiation advocated by the American Society of Nephrology should include information that for the elderly, maintenance dialysis therapy has not been shown to be superior to conservative management (8). In some cases, the dialysis option may be presented as a necessity as opposed to a treatment choice (71). Table 2 gives theoretical issues to discuss with patients to obtain truly informed consent for the joint decision on whether to start dialysis. Patients, when given a choice, may be willing to have fewer days alive, but a better quality of life (72). At least for the elderly, and probably for all patients who are compliant with their predialysis medical regimen, early initiation of dialysis will result in more days in hospital than for patients who are treated with conservative management and delay initiation of dialysis (73).

Conclusions

As early initiation of dialysis has not been shown to be beneficial, dialysis start should be individualized and be delayed until a patient has minimal renal function unless disabling symptoms of renal failure develop. There is little proof that it is dangerous to wait until low levels of GFR are reached to start dialysis. On the other hand, the dangers of dialysis initiation have been well documented and

the Hippocratic precept of "first do no harm" should be taken to heart. Early preparation for dialysis at a later start is encouraged, taking into consideration the observed RFT. Much more work is needed to define the symptoms, signs, and laboratory findings in CKD5 that will facilitate better advice on timing of dialysis initiation. In addition, the initiation of maintenance dialysis after an AKI episode and in CHF needs further study. We conclude that available evidence shows that there is often no need to rush dialysis initiation. It may well be appropriate to describe our view as "Fools rush in where angels fear to tread."

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None declared.

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